



## **Delirium Assessment in Acute Stroke**

### **A Systematic Review and Meta-Analysis of Incidence, Assessment Tools, and Assessment Frequencies**

Stokholm, Jannik; Steenholt, Janni Vagner; Csilag, Claudio; Kjær, Troels Wesenberg; Christensen, Thomas

*Published in:*

Journal of Central Nervous System Disease

*DOI:*

[10.1177/1179573519897083](https://doi.org/10.1177/1179573519897083)

*Publication date:*

2019

*Document version*

Publisher's PDF, also known as Version of record


*Document license:*

[CC BY-NC](#)

*Citation for published version (APA):*

Stokholm, J., Steenholt, J. V., Csilag, C., Kjær, T. W., & Christensen, T. (2019). Delirium Assessment in Acute Stroke: A Systematic Review and Meta-Analysis of Incidence, Assessment Tools, and Assessment Frequencies. *Journal of Central Nervous System Disease*, 11, 1-9. <https://doi.org/10.1177/1179573519897083>

# Delirium Assessment in Acute Stroke: A Systematic Review and Meta-Analysis of Incidence, Assessment Tools, and Assessment Frequencies

Jannik Stokholm<sup>1,2</sup> , Janni Vagner Steenholt<sup>1</sup>, Claudio Csilag<sup>2,3</sup>, Troels Wesenberg Kjær<sup>2,4</sup> and Thomas Christensen<sup>1,2</sup>

<sup>1</sup>Department of Neurology, Nordsjællands Hospital, Hillerød, Denmark. <sup>2</sup>Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark. <sup>3</sup>Psychiatric Outpatient Clinic, Mental Health Centre North Zealand, Hillerød, Denmark. <sup>4</sup>Center for Neurophysiology, Department of Neurology, Zealand University Hospital, Roskilde, Denmark.

Journal of Central Nervous System Disease  
Volume 11: 1–9  
© The Author(s) 2019  
Article reuse guidelines:  
sagepub.com/journals-permissions  
DOI: 10.1177/1179573519897083



## ABSTRACT

**PURPOSE:** The purpose of this systematic literature review was to examine whether different assessment methods contribute to the variance in delirium incidence detected in populations of patients with acute stroke. Specifically, the aim was to address the influence of (1) choice of assessment tool, (2) frequency of assessment, and (3) type of health professional doing the assessment.

**METHODS:** We searched MEDLINE, EMBASE, and PsycINFO and included pro- and retrospective cohort studies assessing delirium during hospitalization of adult acute stroke patients.

**RESULTS:** In 30 articles, 24 unique populations were identified and included in the review. Delirium incidence ranged from 1.4% to 75.6% in total and a chi-square test showed a significant heterogeneity across studies ( $\chi^2 = 536.5$ ,  $df = 23$ ,  $P < .0001$ ). No studies had an assessment for delirium before a patient entered the study. No specific patterns regarding the influence of tool, assessment frequency or health professional were discernible.

**DISCUSSION:** Subgroups analyses were not conducted due to the heterogeneity across studies. Studies comparing delirium assessment tools directly with each other are needed.

**CONCLUSIONS:** Delirium is a common complication in acute stroke. No firm conclusions about a possible correlation of choice of tool, assessment frequency, and delirium incidence could be made due to the great heterogeneity of the study populations. Only 1 study compared 2 tools directly with each other. Further studies comparing delirium assessment tools directly with each other are needed.

**KEYWORDS:** Delirium, delirium assessment, acute stroke

**RECEIVED:** March 13, 2019. **ACCEPTED:** December 2, 2019.

**TYPE:** Systematic Review

**FUNDING:** The authors disclose receipt of the following financial support for the research, authorship, and/or publication of this article: JS is a PhD-student with a salary supported by research grants from 'Nordsjællands Hospital' and 'Familien Hede Nielsens Fond'.

**DECLARATION OF CONFLICTING INTERESTS:** The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**CORRESPONDING AUTHOR:** Jannik Stokholm, Department of Neurology, Nordsjællands Hospital, Dyrehavevej 29, 3400 Hillerød, Denmark. Email: jannik.stokholm.01@regionh.dk

## Introduction

Development of acute delirium is a serious complication in patients hospitalized with acute stroke. Delirium interferes with initiation of stroke rehabilitation and causes prolonged stay in hospital, worse functional outcome after stroke, and increased mortality.<sup>1</sup> In 2012, 2 reviews on the occurrence of delirium in acute stroke reported incidences in the ranges of 10% to 48%<sup>1</sup> and 2.3% to 66%,<sup>2</sup> respectively.

The *DSM-V*<sup>3</sup> is the newest edition of the *Diagnostic and Statistical Manual of Mental Disorders* from the American Psychiatric Association. Previous editions also relevant to this review include the *DSM-IV-TR*, the *DSM-IV*, and the *DSM-III-R*.<sup>4-6</sup> The definition of delirium is the same in *DSM-IV-TR* and the *DSM-IV* and differs only slightly from the definition in the *DSM-V*.

The DRS (Delirium Rating Scale) is a 10-item scale made to rate the severity of delirium symptoms.<sup>7</sup> The original version is from 1988 with a later revision in 1998 (the Delirium

Rating Scale Revised 1998 [DRS-R-98]). The DRS-R-98 consists of a 13-item symptom severity scale and 3 additional diagnostic items.<sup>8</sup> Both scales are intended to be completed by a clinician using all available information about the patient under assessment.

The Confusion Assessment Method (CAM) was developed to provide an easy-to-use tool to health staff members not specifically trained in psychiatry.<sup>9</sup> The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) is an edition of the CAM designed for use in the intensive care setting.<sup>10</sup>

In patients with stroke, the diagnosis of delirium is complicated by the fact that acute stroke itself as well as dementia caused by previous vascular events may cause delirium-like symptoms differing only in time of onset and development. In addition, the symptoms and signs of delirium have a fluctuating course over hours and days. It may therefore be difficult for unexperienced observers to correctly identify delirium. Some classes of health professionals may also be better equipped than



others in the assessment of delirium and this may affect a given tool's ability to identify delirium. Furthermore, it is possible that the frequency of assessments will influence the number of delirious patients found.

The purpose of this systematic literature review was to examine whether different assessment methods contribute to the variance in delirium incidence. Specifically, the aim was to address the influence of (1) choice of assessment tool, (2) frequency of assessment, and (3) type of health professional doing the assessment. It was not the purpose of this review to evaluate studies directly comparing 2 or more tools with each other.

## Methods

A protocol for this review was published online at the PROSPERO register (ID CRD42017068360).<sup>11</sup> The protocol was based on the PRISMA-P guidelines.<sup>12</sup> The article has been written in accordance with the PRISMA guidelines.<sup>13</sup>

As described in detail in the systematic review protocol, we searched the databases MEDLINE, EMBASE, and PsycINFO. A health science librarian was consulted on the search strategy. The Medical Subject Headings (MeSH terms) 'stroke', 'cerebrovascular disorders', 'delirium', 'confusion' were searched in combination with the words 'cerebrovascular syndrome', 'brain ischemia', 'brain vascular accident', 'cerebrovascular accident', 'confusional state', 'psychosyndrome', 'brain syndrome', 'metabolic encephalopathy'. See review protocol for the exact MEDLINE search string.<sup>11</sup> The searches at EMBASE and PsycINFO were built on the same search words. No date restrictions were imposed on any of the searches and all searches were finalized in August 2017.

Screening, data extraction, and risk of bias assessments were done independently by 2 reviewers (J.S. and J.V.S.) and consensus established. Disagreement was sought to be resolved through discussion between J.S. and J.V.S. If consensus could not be reached, a third reviewer (T.C.) resolved the disagreement.

Study designs eligible for the review were prospective and retrospective observational cohort studies. Study designs excluded from the review were interventional studies, observational studies other than cohort studies, studies with 3 or less patients, and reviews.

To be included, studies had to estimate the delirium incidence, that is, new cases of delirium found during the study period, in a population of patients  $\geq 18$  years of age admitted with acute stroke as hospital inpatients. Stroke populations with any combination of ischaemic stroke, intracerebral haemorrhages and subarachnoid haemorrhages were eligible. So were populations of patients with symptoms lasting less than 24 hours if they had relevant acute lesions on cerebral imaging. Patients with transient ischaemic attacks without demonstrable acute brain damage on brain imaging were excluded as they had full remission of symptoms and constituted a group which was treated heterogeneously, for example, in some institutions, these patients were admitted to an acute stroke wards and at other places they were handled via outpatient clinics. If a study

encompassed patients both fulfilling and not fulfilling the inclusion criteria and the data from the patients fulfilling the inclusion criteria could be extracted for separate analysis, the study was considered eligible.

A 95% confidence interval (CI) for each study's delirium incidence was calculated. The chi square test of heterogeneity was performed and due to significant heterogeneity the DerSimonian and Laird Random Effects Model<sup>14</sup> was used to synthesize the overall delirium incidence estimate. Note that in the DerSimonian and Laird Random Effects Model each study is given a weight based on the number of patients, but the range of weights are compressed as compared with a fixed effects model. Data storage, analyses, and figures were done in Microsoft Excel and RStudio (©2009-2017 RStudio, Inc, Boston, MA, USA).

## Results

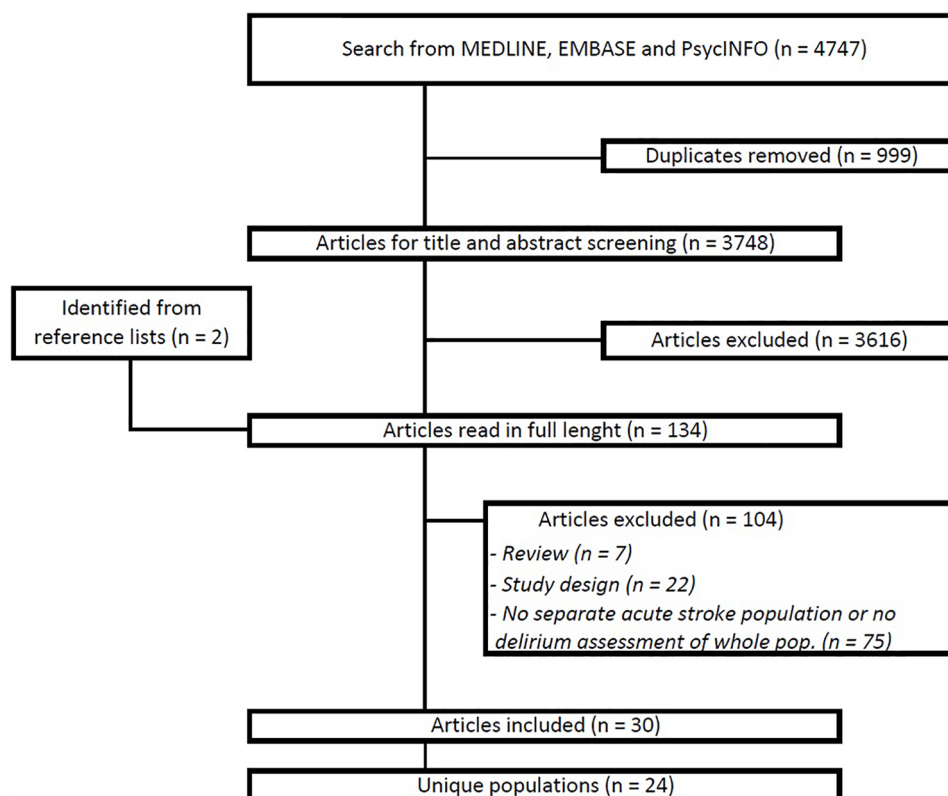
A total of 3748 unique titles were identified. A total of 134 articles were read in full length and 30 were included in the review.<sup>15-44</sup> In these 30 articles, 24 unique populations were identified (Figure 1). The discrepancy between the number of articles and the number of unique populations was caused by the fact that the same population was described in more than one article. Thus, 2 populations were described in 2 separate articles and 2 populations were reported on in 3 separate articles. The included studies were published during the years 1987 to 2017 and consisted of 2 retrospective and 22 prospective cohort studies. Table 1 is an overview of the included studies. A total of 21 studies reported a mean for age which was in the range of 51 to 79.2 years. The median age (range of 68-74 years) was available for those 3 studies which did not report a mean age.

### Delirium incidence

The delirium incidence range was 1.4% to 75.6% (see Figure 2). Figure 3 shows a graphic representation of the data synthesis for the delirium incidence. The chi-square test showed a significant heterogeneity across studies ( $\chi^2 = 536.5$ ,  $df = 23$ ,  $P < 0.0001$ ). Cochrane  $Q = 743.5$  ( $P < .0001$ ) and  $I^2 = 96.9\%$  and the random effects model showed a delirium incidence of 22.8%, 95% CI: 18.2-27.4 (23.9%, 95% CI: 19.5-28.4%, with the 2 retrospective studies removed from the model).

### Assessment tools

In 16 studies, the tools used were the CAM, CAM-ICU, DRS, and DRS-R-98 (exclusively, in combination with each other or in combination with *DSM* criteria). The study by McManus et al<sup>40</sup> reported 2 delirium incidences for the same population; one for the DRS (delirium incidence 26.8%) and one for the CAM (delirium incidence 28.1%). Six studies solely used some version of the *DSM* criteria (1 used *DSM-V*, 3 used *DSM-IV* or *DSM-IV-TR*, and 2 used *DSM-III-R* criteria) and 2 studies used some other specified criteria for delirium (see Table 1).



**Figure 1.** Flowchart of the search and article selection process.

Looking only at the studies using the CAM, CAM-ICU, DRS, and DRS-R-98 (alone or in combinations with each other or in combination with *DSM* criteria), the delirium incidences were within a narrower range of 6.6% to 35.3% (Figure 2).

#### *Frequency and timing of assessment tool use*

In the prospective studies, delirium assessment was done once a day or more in 6 studies. The remaining 16 prospective studies assessed with a smaller frequency, for example, twice a week. The retrospective studies used patient records, either covering the entire admission or limited to days 1 through 7.

Marked in green in Table 1 are the 11 prospective studies that assessed roughly once a day (eg, daily except Sundays) or more often. Looking at the table, comparing these 11 studies with those that assessed with a frequency less than roughly daily, there is no discernible pattern with respect to delirium incidence.

#### *Type of health professional*

Information about the type of health professional(s) using a specific tool was available from 20 studies (see Table 1). Study authors were contacted on 8 occasions to clarify the information about which type of health professional had done the delirium assessments in their studies. Nine prospective studies specifically stated that the persons using the tools had been trained to use their specific tool or to apply the delirium

criteria. No specific pattern as to whether the type of health professional doing the assessments had an influence on the delirium incidence was discernible.

#### *Quality assessment*

A panel of questions was designed to perform a quality assessment of the included studies. The questions were taken from Watt et al<sup>45</sup> and were, for some questions, modified slightly. Questions on exclusion of aphasic patients, delirium assessment before inclusion into a study, and the timeframes used for delirium assessments were added. Table 2 shows the questions and the answers for each study in this review. Of the 24 studies, 5 did not have clearly described characteristics regarding age, disease status, and preexisting cognitive impairment. The recruitment strategy was nonconsecutive in one population and unclear in another three. The inclusion and exclusion criteria were judged not to allow for appropriate selection of the respective studies' target populations in 2 cases (unclear in 3 cases) and aphasic patients were excluded in 9 studies. There were missing data on delirium assessments in 11 studies and 2 of these did not document reasons for this missing data. The delirium assessment was not performed by an independent assessor in 8 studies (unclear in an additional 6 studies) but only in 2 studies were the delirium assessments not done in a standard manner. No studies had an assessment negative for delirium before a patient entered the study and only 2 studies described the time frame used for a given tool's application.

**Table 1.** Summary of included studies.

STUDY AND YEAR	COUNTRY	STROKE TYPES	SIZE (N)	AGE, Y: MEAN (SD), RANGE	STUDY DESIGN	DELIRIUM CONSIDERED PRESENT IF	FREQUENCY AND TIMING OF TOOL USE	TYPES OF HEALTH PROFESSIONALS USING THE TOOL	DELIRIUM INCIDENCE, %
Reijneveld et al. <sup>26</sup>	Netherlands	SAH	646	51, 34-66 <sup>a</sup>	Retrospective	Prespecified criteria for ACS fulfilled <sup>b</sup>	Patient records from time of admission	Not disclosed	1.4
Melkas et al. <sup>22</sup>	Finland	AIS	263	70.8 (7.4), 55-85	Retrospective	DSM-IV criteria fulfilled	Medical records and nurses' notes from between days 1 and 7	A senior psychiatrist	19
Lim et al. <sup>15</sup>	Republic of Korea	AIS	576	65.2, 23-93	Prospective	CAM to screen, if positive then evaluation with DRS-R-98 <sup>c</sup>	Daily	Not disclosed	6.6
Dahl et al. <sup>23</sup>	Norway	AIS, ICH, SAH	178	73	Prospective	CAM to screen, if positive then evaluation with DSM-IV	CAM was used twice daily	CAM used by nurses, DSM-IV criteria applied by a neurologist	10.1
Alvarez-Perez and Paiva <sup>17</sup>	Portugal	AIS, haemorrhage	1072	Median 68, Q1: 77, Q3: 83	Prospective	DSM-V criteria fulfilled	Near continuously observed	Nurses and other medical staff	11
Caeiro et al. <sup>44</sup>	Portugal	AIS, ICH	190	Delirium group: 63.6 (12.8), 33-84	Prospective	DRS score of $\geq 10$ points and DSM-IV-TR criteria fulfilled	Day 1 whenever possible	A psychologist	11.6
Oldenbeuving et al. <sup>36</sup>	Netherlands	AIS, ICH	527	72, 29-96	Prospective	CAM positive	Between days 2 and 4 and again between days 5 and 7	Neurological residents	11.8
Lees et al. <sup>19</sup>	UK	AIS, haemorrhage	101	Median 74, IQR: 64-85 <sup>d</sup>	Prospective	CAM positive	Once between days 1 and 4 after admission	Four medical students undertaking a period of elective study in stroke	11.9
Oldenbeuving et al. <sup>33</sup>	Netherlands	AIS, ICH	273	72, 31-99	Prospective	CAM positive	Between days 2 and 4 and again between days 5 and 7	MD	15
Caeiro et al. <sup>42</sup>	Portugal	SAH	68	55.5 (14.5), 27-86	Prospective	DRS score of $\geq 10$ points and DSM-IV-TR criteria fulfilled	Day 1 whenever possible (all patients were scored within the first 4 days)	A psychologist	16.2
Kozak et al. <sup>31</sup>	Turkey	AIS	60	66.2 (12.5), 31-89	Prospective	DRS score of $\geq 10$ points and DSM-IV criteria fulfilled	Daily	Same psychiatrist for every patient	18.3
Hénon et al. <sup>27</sup>	France	AIS, ICH	202	75, 42-101	Prospective	DRS score of $\geq 10$ points	Day 1 and 2 for all, repeated if clinical change	Neurologist	24.3
Sheng et al. <sup>25</sup>	Australia	AIS, ICH	156	79.2 (6.7)	Prospective	DSM-IV criteria fulfilled	Once within 3 days of admission	Same MD for all patients	25
Dostović et al. <sup>24</sup>	Bosnia and Herzegovina	AIS, ICH, SAH	233	70 (11.3)	Prospective	DRS-R-98 score $> 16$ points and DSM-IV criteria fulfilled	Once within 4 days after stroke onset	A neuropsychiatrist	25.3

(Continued)



Table 1. (Continued)

STUDY AND YEAR	COUNTRY	STROKE TYPES	SIZE (N)	AGE, Y: MEAN (SD), RANGE	STUDY DESIGN	DELIRIUM CONSIDERED PRESENT IF	FREQUENCY AND TIMING OF TOOL USE	TYPES OF HEALTH PROFESSIONALS USING THE TOOL	DELIRIUM INCIDENCE, %
Miu and Yeung <sup>20</sup>	China	AIS, ICH, SAH	314	72.9 (10.3), 50-94	Prospective	CAM positive	Daily between days 1 and 5	Same geriatrician for all patients	27.4
Kara et al. <sup>21</sup>	Turkey	AIS, ICH, SAH	150	Delirium group: 68 (1.9), Non-delirium group: 61.2 (1.3)	Prospective	DRS score of $\geq 10$ points and DSM-IV-TR criteria fulfilled	Close monitoring the first 5 days	Not disclosed	28
McManus et al. <sup>41</sup>	UK	AIS, ICH	82	66.4 (15.9), 24-97	Prospective	CAM positive or DRS score of $\geq 10$ points	First assessment within first 4 days and then weekly until a max. of 4 weeks or discharge	One assessor – a senior Registrar in Geriatric Medicine	CAM: 28.1 DRS: 26.8
Olsson et al. <sup>29</sup>	Sweden	AIS	16	71 (11)	Prospective	DSM-III-R criteria fulfilled	Repeated assessments between days 3 and 7	MDs	31.3
Naidech et al. <sup>32</sup>	USA	ICH	98	63 (13.8) <sup>e</sup>	Prospective	CAM-ICU positive	Twice daily	ICU nurses	31.6
Ojagbemi et al. <sup>16</sup>	Nigeria	AIS, haemorrhage	99	61.1 (12.9)	Prospective	CAM positive or DRS score of $\geq 10$ points	Two assessments within the first 7 days of admission (a maximum of 4 days between assessments)	CAM: A research assistant. DRS: A psychiatrist	33.3
Rosenthal et al. <sup>19</sup>	USA	ICH	150	63.5 <sup>f</sup>	Prospective	CAM-ICU positive	Twice daily	Nursing staff	35.3
Fassbender et al. <sup>28</sup>	Germany	AIS	23	Median 72, range 39-89	Prospective	DSM-III-R criteria fulfilled	Observations during the first days of hospitalization	Not disclosed	39.1
Mitasova et al. <sup>38</sup>	Czech Republic	AIS, ICH	129	71.2 (11.5), 30-93	Prospective	DSM-IV criteria fulfilled	Daily except Sundays	A team of at least 1 neurologist and 1 neuropsychologist, if necessary also a psychiatrist and/or a speech therapist	42.6
Mori and Yamadori <sup>30</sup>	Japan	AIS	41	68.2 (10.9), 18-85	Prospective	Prespecified criteria for ACS or AAD fulfilled <sup>g</sup>	Within 2 weeks of onset	Staff neurologists	75.6

Abbreviations: AAD, acute agitated delirium; ACS, acute confusional state; AIS, acute ischaemic stroke; CAM, Confusion Assessment Method; CAM-ICU, Confusion Assessment Method for the intensive care unit; DRS, Delirium Rating Scale; DRS-R-98, Delirium Rating Scale Revised 1998; DSM-III-R, *Diagnostic and Statistical Manual of Mental Disorders* (Third Edition Revised); DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition); DSM-IV-TR, *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition, Text Revision); DSM-V, *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition); ICH, intracerebral haemorrhage; ICU, intensive care unit; MD, medical doctor; SAH, subarachnoid haemorrhage.

<sup>a</sup>Only data on age of the ACS patients were reported.

<sup>b</sup>ACS was defined as (a) a sudden disturbance of consciousness, manifested by a reduced clarity of awareness, together with (b) a change in cognition, including memory impairment, language disturbances, and disorientation to time or place.

<sup>c</sup>Not specified if any specific score triggered a delirium diagnosis or if the 3 additional diagnostic items were used to indicate whether delirium was present or not.

<sup>d</sup>Only 101 patients were ever delirium assessed but the reported ages are from the total 111 patients (10 patients were never assessed for nondisclosed reasons).

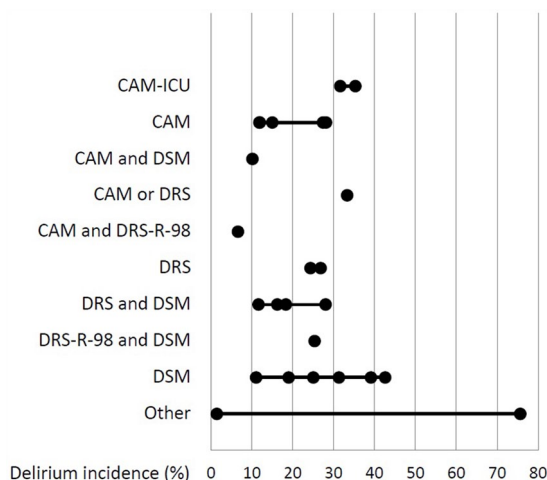
<sup>e</sup>Only 98 patients were ever delirium assessed but the reported ages are from the total 114 patients (16 patients were never assessed because of persistent coma).

<sup>f</sup>Only 150 were ever delirium assessed but the reported ages are from the total 174 patients (24 patients were not assessed due to neurologic injury).

<sup>g</sup>ACS is failure to maintain a coherent stream of thought or action with inattention and distractibility and ACS causes characteristic cognitive impairments such as disorientation, memory disturbance, unconcern of illness, aphasia, anomia, and constructional disability. AAD have the same features plus vivid hallucinations, delusion, and affective and autonomic excitement.

## Discussion

In our review, we found a large range in delirium incidences from 1.4% to 75.6%. It must be emphasized that none of the studies tested a certain screening method against a predefined golden standard. The study by Mitasova et al<sup>38</sup> was a study



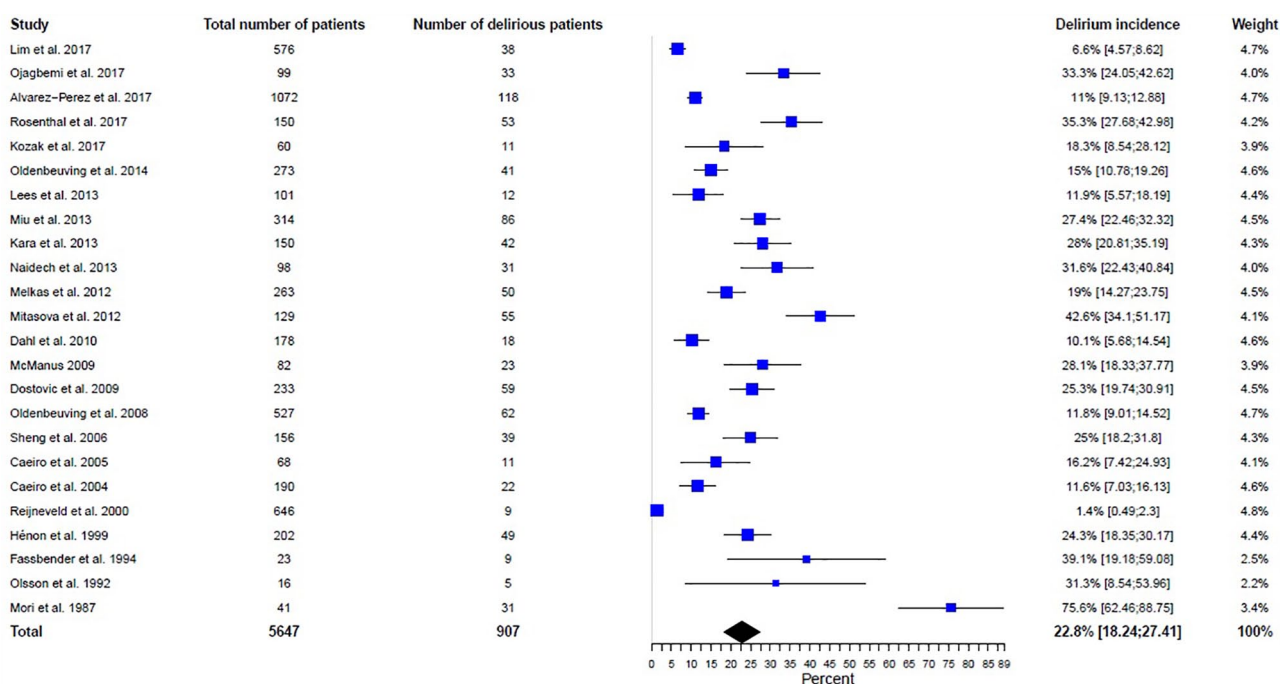
**Figure 2.** Figure illustrating the delirium incidences categorized according to which assessment tools were used in each of the studies. Note that there are 4 studies using solely the CAM, 2 studies found incidences of 27.4% and 28.1%, respectively, and are almost nondiscernible from each other on the figure. Please note that the study by McManus et al is depicted twice, once for the CAM (delirium incidence 28.1%) and once for the DRS (delirium incidence 26.8%). Abbreviations: CAM, Confusion Assessment Method; CAM-ICU, Confusion Assessment Method for the intensive care unit; RS, Delirium Rating Scale; DRS-R-98, Delirium Rating Scale Revised 1998; DSM, *Diagnostic and Statistical Manual of Mental Disorders* (any edition).

comparing blinded assessments between a Czech version of the CAM-ICU and the *DSM-IV*; however, they reported delirium incidence for the *DSM-IV* only and therefore only this was included into this review. Based on the data in the included studies, we were able to calculate an overall estimate of delirium incidence of approximately 23%.

Even though all populations are acute stroke populations, heterogeneity across populations should be assumed. We did not do any test for a potential statistically significant difference between subgroups (ie, studies using the CAM, DRS, or DRS-R-98 vs the rest) as the studies were of observational design and the heterogeneity was, as mentioned, significant. This means that the subgroup pooled estimates and  $I^2$  values might very well have turned out to be different for other reasons than the chosen subgrouping because of unknown confounders and any confident conclusions of such tests would therefore be impossible to make.

However, the narrower range of incidences from studies using the CAM, CAM-ICU, DRS, or DRS-R-98 generates the hypothesis that using standardized and validated delirium assessment tools such as the CAM, CAM-ICU, DRS, or DRS-R-98, a more precise detection of acute delirium may be obtained in patients with acute stroke. We emphasize that results from this review do not allow actual comparison of groups of studies with each other due to the heterogeneity of the studies. Only one study in this review compared 2 tools directly with each other. Further studies comparing delirium assessment tools directly with each other are needed.

A study by Infante et al<sup>46</sup> was not included into this review, because it had patients with transient ischaemic attack



**Figure 3.** Forest plot. The size of each square visualizes a study's percentile weight, the horizontal bars indicate the 95% confidence interval (CI), the centre of the diamond indicates the overall delirium incidence estimate, and the width of the diamond represents the 95% CI of the overall estimate.

Table 2. Quality assessment table.

	WERE THE CHARACTERISTICS (AGE, DISEASE STATUS, CONSIDERATION OF PREEXISTING COGNITIVE IMPAIRMENT) OF PATIENTS CLEARLY DESCRIBED?	WAS THE RECRUITMENT STRATEGY CONSECUTIVE?	DID THE INCLUSION AND EXCLUSION CRITERIA ALLOW FOR APPROPRIATE SELECTION OF THE TARGET POPULATION FOR THE STUDY?	EXCLUSION OF APHASIC PATIENTS?	WAS THERE ADEQUATE DOCUMENTATION FOR REASONS OF MISSING DATA (SKIP IF QUESTION NOT APPLICABLE)?	WAS THE DELIRIUM ASSESSMENT PERFORMED BY AN INDEPENDENT ASSESSOR (IE, NOT A MEMBER OF THE CARE TEAM)?	WAS THE DELIRIUM ASSESSMENT DONE IN A STANDARD MANNER FOR ALL PARTICIPANTS?	WAS THERE AN ASSESSMENT NEGATIVE BEFORE PATIENTS ENTERED THE STUDY?	WAS THE TIME FRAME FOR THE TOOL APPLICATION DESCRIBED?
Reijneveld et al. <sup>26</sup>	Yes	Yes	No	No	Yes	Yes	Yes	No	No
Melkas et al. <sup>22</sup>	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes
Lim et al. <sup>15</sup>	Yes	Yes	Unclear	No	NA	Unclear	Yes	No	No
Dahl et al. <sup>23</sup>	Yes	Yes	Yes	No	Yes	No	Yes	No	No
Alvarez-Perez and Paiva <sup>17</sup>	No	Unclear	Yes	No	NA	No	Yes	No	No
Caeiro et al. <sup>44</sup>	Yes	Yes	Yes	No	No	Yes	Yes	No	No
Oldenbeuving et al. <sup>36</sup>	Yes	Yes	Yes	No	Yes	No	Yes	No	No
Lees et al. <sup>19</sup>	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No
Oldenbeuving et al. <sup>33</sup>	Yes	Yes	Yes	Yes	NA	No	Yes	No	No
Caeiro et al. <sup>42</sup>	Yes	Yes	Yes	No	NA	Yes	Yes	No	No
Kozak et al. <sup>31</sup>	No	Yes	Yes	Yes	NA	Yes	Yes	No	No
Hénon et al. <sup>27</sup>	Yes	Yes	No	No	NA	Unclear	Yes	No	No
Sheng et al. <sup>25</sup>	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes
Dostović et al. <sup>24</sup>	Yes	Yes	Yes	Yes	NA	Unclear	Yes	No	No
Miu and Yeung <sup>20</sup>	Yes	Yes	Unclear	No	NA	Unclear	Yes	No	No
Kara et al. <sup>21</sup>	Yes	Yes	Yes	Yes	NA	Unclear	Yes	No	No
McManus et al. <sup>41</sup>	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No
Olsson et al. <sup>29</sup>	No	No	Unclear	No	NA	Yes	Yes	No	No
Naidech et al. <sup>32</sup>	Yes	Yes	Yes	No	Yes	No	Yes	No	No
Ojagbemi et al. <sup>16</sup>	Yes	Yes	Yes	Yes	NA	Yes	Yes	No	No
Rosenthal et al. <sup>18</sup>	No	Unclear	Yes	No	Yes	No	Yes	No	No
Fassbender et al. <sup>28</sup>	No	Unclear	Yes	No	NA	Unclear	No	No	No
Mitasova et al. <sup>38</sup>	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No
Mori and Yamadori <sup>30</sup>	Yes	Yes	Yes	Yes	NA	No	No	No	No

Abbreviation: NA, not applicable.



(symptoms lasting less than 24 hours and no acute cerebral lesions demonstrated on imaging) intermixed in its population but is still worth mentioning. The study found a delirium incidence of 52% when using the 4AT instrument but a lower incidence of 32% when the *DSM-V* criteria were applied to the same patients by the same neurologist. The 4AT was available for the first time in 2011 and is designed as an instrument for rapid delirium screening.<sup>47</sup>

Concerning the types of health professionals using the tools and the delirium incidence found, no discernible pattern was evident from our review. As mentioned above, the heterogeneity among the studies was considerable and no subgroup analyses were therefore done. To our knowledge, no previous studies have specifically addressed the possible influence of the type of health professional on the detection rate of delirium. Yet, this question must remain unanswered.

Due to the fluctuating symptoms of delirium, it could be speculated that the frequency of assessments will have an impact on the detection rate of delirium. However, due to the multitude of different tools in use across these 22 prospective studies, no firm conclusions can be made for any of the tools as to whether there is a correlation between the frequency and delirium detection.

Several sources for bias may exist. An important bias is the fact that the studies had clearly different types of settings and spanned a rather wide range of publication years. For example, some were conducted in modern stroke wards, others in neurological semi-intensive care units and others again in older settings. The types of stroke also differed across studies. Some reported both on ischaemic and haemorrhagic strokes, others only one type. The underlying stroke etiology itself might also in some situations contribute to the development of delirium. Another potential bias may come in- or exclusion of aphasic patients. The exclusion of aphasic patients may result in a lower incidence of delirium. Thought content and attention may be harder to judge when language is impaired, and this makes severely aphasic patients more difficult to assess for delirium. A validated tool for assessing severely aphasic patients is obviously needed. The CAM-ICU<sup>10</sup> does not require the patient to speak but severe aphasia might still interfere with patient's ability to understand what is being said without confusion being present. In addition, perceptual deficits other than aphasia might also make a delirium assessment difficult. Data on perceptual deficits other than aphasia were not collected in this review.

Assessment for delirium before the patients entered a given study was not done in any of the included studies. It is quite conceivable that some patients might have been delirious before inclusion (and before admission or before their stroke). Another bias might come from the time frames used when evaluating patients for the presence of delirium. For a given tool, some studies might consistently have used longer time frames (eg, looking back 24 hours instead of 8 hours) than others. The effect this might have on the incidence of delirium is unknown.

## Conclusions

Delirium is a common complication in acute stroke. The wide ranges of delirium incidence reported in the different stroke studies imply that delirium can be difficult to recognize in patients with stroke, leading to both under- and overdiagnosis.

No firm conclusions about a possible correlation of choice of tool, assessment frequency, and delirium incidence could be made due to the great heterogeneity of the study populations. Only 1 study compared 2 tools directly with each other. Further studies comparing delirium assessment tools directly with each other are needed.

## Acknowledgements

The authors wish to thank Jette Meelby, health science librarian at Nordsjællands Hospital, for her help constructing the search strings and procuring articles. They also wish to thank Jacob Mesot Liljehult, RN, cand.scient.san., PhD fellow at Nordsjællands Hospital, for help with the forest plot.

## Author Contributions

JS and JVS researched literature. JS, JVS, and TC conceived the study. All authors were involved in protocol development and data analysis. JS wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

## Ethical approval

Ethical approval was not sought for this article because there was no indication that any of the studies in review posed any ethical dilemma.

## Informed consent

Informed consent was not sought for this article because no patient identifiable data were obtained for this review from any of the studies reviewed. All studies included into the review featured anonymized patient data.

## Guarantor

J.S. is the guarantor of this study.

## ORCID iD

Jannik Stokholm  <https://orcid.org/0000-0003-3300-1504>

## REFERENCES

1. Shi Q, Presutti R, Selchen D, Saposnik G. Delirium in acute stroke: a systematic review and meta-analysis. *Stroke*. 2012;43:645-649.
2. Carin-Levy G, Mead GE, Nicol K, Rush R, van Wijck F. Delirium in acute stroke: screening tools, incidence rates and predictors: a systematic review. *J Neurol*. 2012;259:1590-1599.
3. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*. Washington, DC: American Psychiatric Association; 2013.
4. American Psychiatric Association. Chapter on Delirium, Dementia, and Amnesic and Other Cognitive Disorders. In: *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition Text Revision (DSM-IV-TR)*; 2000. <https://behavetnet.com/apa-diagnostic-classification-dsm-iv-tr>.
5. American Psychiatric Association. Chapter on Delirium, Dementia, and Amnesic and Other Cognitive Disorders. In: *Diagnostic and Statistical Manual*

- of *Mental Disorders, 4th Edition (DSM-IV)*; 1994. [https://www.brown.edu/Courses/BI\\_278/Other/Teaching%20examples/Brain%20and%20Behavior/articles/dementia.pdf](https://www.brown.edu/Courses/BI_278/Other/Teaching%20examples/Brain%20and%20Behavior/articles/dementia.pdf).
6. American Psychiatric Association. Chapter on Organic Mental Syndromes and Disorders. In: *Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition – Revised (DSM-III-R)*; 1987. <https://searchworks.stanford.edu/view/1693090>.
7. Trzepacz PT, Baker RW, Greenhouse J. A symptom rating scale for delirium. *Psychiatry Res.* 1988;23:89-97.
8. Trzepacz PT, Mittal D, Torres R, Canary K, Norton J, Jimerson N. Validation of the Delirium Rating Scale-revised-98: comparison with the delirium rating scale and the cognitive test for delirium. *J Neuropsychiatry Clin Neurosci.* 2001;13:229-242.
9. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegel AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med.* 1990;113:941-948.
10. Ely EW, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med.* 2001;29:1370-1379.
11. Stokholm J, Steenholt JV, Christensen T. Delirium screening in acute stroke: a systematic review and meta-analysis of incidence, screening tools and screening frequencies – review protocol. [http://www.crd.york.ac.uk/PROSPERO/display\\_record.php?ID=CRD42017068360](http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017068360).
12. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev.* 2015;4:1.
13. Moher D, Liberati A, Tetzlaff J, Altman DG, for PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6:e1000097.
14. Deeks JJ, Altman DG, Bradburn MJ. Chapter 15: statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Smith GD, Altman DG, eds. *Systematic Reviews in Health Care: Meta-Analysis in Context*, 2nd ed. Oxford: John Wiley;2001:285-312.
15. Lim TS, Lee JS, Yoon JH, et al. Cigarette smoking is an independent risk factor for post-stroke delirium. *BMC Neurol.* 2017;17:56.
16. Ojagbemi A, Owolabi M, Bello T, Baiyewu O. Stroke severity predicts post-stroke delirium and its association with dementia: longitudinal observation from a low income setting. *J Neurol Sci.* 2017;375:376-381.
17. Alvarez-Perez FJ, Paiva F. Prevalence and risk factors for delirium in acute stroke patients. *J Stroke Cerebrovasc Dis.* 2017;26:567-573.
18. Rosenthal LJ, Francis BA, Beaumont JL, et al. Agitation, delirium, and cognitive outcomes in intracerebral hemorrhage. *Psychosomatics.* 2017;58:19-27.
19. Lees R, Corbet S, Johnston C, Moffitt E, Shaw G, Quinn TJ. Test accuracy of short screening tests for diagnosis of delirium or cognitive impairment in an acute stroke unit setting. *Stroke.* 2013;44:3078-3083.
20. Miu DK, Yeung JC. Incidence of post-stroke delirium and 1-year outcome. *Geriatr Gerontol Int.* 2013;13:123-129.
21. Kara H, Bıçakcı S, Over MF, et al. Acute confusional state at early stage of stroke [in Turkish]. *J Neurol Sci.* 2013;30:21-29.
22. Melkas S, Laurila JV, Vataja Oksala N, et al. Post-stroke delirium in relation to dementia and long-term mortality. *Int J Geriatr Psychiatry.* 2012;27:401-408.
23. Dahl MH, Rønning OM, Thommessen B. Delirium in acute stroke – prevalence and risk factors. *Acta Neurol Scand Suppl.* 2010;190:39-43.
24. Dostovic Z, Smajlović D, Sinanović O, Vidović M. Duration of delirium in the acute stage of stroke. *Acta Clin Croat.* 2009;48:13-17.
25. Sheng AZ, Shen Q, Cordato D, Zhang YY, Yin Chan DK. Delirium within three days of stroke in a cohort of elderly patients. *J Am Geriatr Soc.* 2006;54:1192-1198.
26. Reijneveld JC, Wermer M, Boonman Z, van Gijn J, Rinkel GJ. Acute confusional state as presenting feature in aneurysmal subarachnoid hemorrhage: frequency and characteristics. *J Neurol.* 2000;247:112-116.
27. Hénon H, Lebert F, Durieu I, et al. Confusional state in stroke: relation to pre-existing dementia, patient characteristics, and outcome. *Stroke.* 1999;30:773-779.
28. Fassbender K, Schmidt R, Mössner R, Daffertshofer M, Hennerici M. Pattern of activation of the hypothalamic-pituitary-adrenal axis in acute stroke. Relation to acute confusional state, extent of brain damage, and clinical outcome. *Stroke.* 1994;25:1105-1108.
29. Olsson T, Marklund N, Gustafson Y, Nasman B. Abnormalities at different levels of the hypothalamic-pituitary-adrenocortical axis early after stroke. *Stroke.* 1992;23:1573-1576.
30. Mori E, Yamadori A. Acute confusional state and acute agitated delirium. Occurrence after infarction in the right middle cerebral artery territory. *Arch Neurol.* 1987;44:1139-1143.
31. Kozak HH, Uğuz F, Kılınc I, et al. Delirium in patients with acute ischemic stroke admitted to the non-intensive stroke unit: incidence and association between clinical features and inflammatory markers. *Neurol Neurochir Pol.* 2017;51:38-44.
32. Naidech AM, Beaumont JL, Rosenberg NF, et al. Intracerebral hemorrhage and delirium symptoms. Length of stay, function, and quality of life in a 114-patient cohort. *Am J Respir Crit Care Med.* 2013;188:1331-1337.
33. Oldenbeuving AW, de Kort PL, van Eck van der Sluijs JF, Kappelle LJ, Roks G. An early prediction of delirium in the acute phase after stroke. *J Neurol Neurosurg Psychiatry.* 2014;85:431-434.
34. Oldenbeuving AW, de Kort PL, Kappelle LJ, van Duijn CM, Roks G. Delirium in the acute phase after stroke and the role of the apolipoprotein E gene. *Am J Geriatr Psychiatry.* 2013;21:935-937.
35. Oldenbeuving de Kort PL, Jansen BP, Algra A, Kappelle LJ, Roks G. Delirium in the acute phase after stroke: incidence, risk factors, and outcome. *Neurology.* 2011;76:993-999.
36. Oldenbeuving AW, de Kort PL, Jansen BP, Kappelle LJ, Roks G. A pilot study of rivastigmine in the treatment of delirium after stroke: a safe alternative. *BMC Neurol.* 2008;8:34.
37. Kostalova M, Bednarik J, Mitasova A, et al. Towards a predictive model for post-stroke delirium. *Brain Inj.* 2012;26:962-971.
38. Mitasova A, Kostalova M, Bednarik J, et al. Poststroke delirium incidence and outcomes: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med.* 2012;40:484-490.
39. Mc Manus JT, Pathansali R, Ouldred E, Stewart R, Jackson SH. Association of delirium post-stroke with early and late mortality. *Age Ageing.* 2011;40:271-274.
40. McManus J, Pathansali R, Hassan H, et al. The evaluation of delirium post-stroke. *Int J Geriatr Psychiatry.* 2009;24:1251-1256.
41. McManus J, Pathansali R, Hassan H, et al. The course of delirium in acute stroke. *Age Ageing.* 2009;38:385-389.
42. Caeiro L, Menger C, Ferro JM, Albuquerque R, Figueira ML. Delirium in acute subarachnoid haemorrhage. *Cerebrovasc Dis.* 2005;19:31-38.
43. Caeiro L, Ferro JM, Claro MI, Coelho J, Albuquerque R, Figueira ML. Delirium in acute stroke: a preliminary study of the role of anticholinergic medications. *Eur J Neurol.* 2004;11:699-704.
44. Caeiro L, Ferro JM, Albuquerque R, Figueira ML. Delirium in the first days of acute stroke. *J Neurol.* 2004;251:171-178.
45. Watt CL, Momoli F, Ansari MT, et al. The incidence and prevalence of delirium across palliative care settings: a systematic review. *Palliat Med.* 2019;33:865-877.
46. Infante MT, Pardini M, Balestrino M, et al. Delirium in the acute phase after stroke: comparison between methods of detection. *Neurol Sci.* 2017;38:1101-1104.
47. The 4AT Test Group. 4AT test materials and scoring; 2011. <https://www.the4at.com/>. Accessed January 11, 2018.